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THE VASCULAR PROCESSES IN THE
SHWARTZMAN PHENOMENON AS
OBSERVED IN PULMONARY
REACTIONS

A DISSERTATION SUBMITTED TO THE FAC-
ULTY OF THE DIVISION OF THE BIOLOGI-
CAL SCIENCES IN CANDIDACY FOR THE
DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF PATHOLOGY

1937

By
JOHN MARSHALL WEIR

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THE VASCULAR PROCESSES IN THE SHWARTZMAN PHENOMENON AS OBSERVED IN PULMONARY REACTIONS

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The factors controlling the Shwartzman phenomenon are not clearly understood, and, although several views have been presented in the literature, none has clearly defined the underlying mechanism or the site of the reaction. It is the purpose of this paper to report studies along this line and to point out certain features which may throw some light on the nature of the reaction.

There are at present two interpretations of the reaction. One group of workers maintains that the lesions produced in the skin are due to the primary toxicity of the filtrate (1, 2). Gerber (3, 4), however, could not find any parallelism between the degree of inflammation produced in the cutaneous site and the severity of the resulting reaction. Furthermore, he was able to neutralize the preparatory factors without altering the inflammatory factors that are set in action by the preparatory injection. The second group concludes that the reaction is a type of vascular allergy, either an ordinary anaphylactic reaction or one of altered reactivity of blood vessels. Shwartzman (5) suggested that the preparatory injection produces a state of hypervulnerability in the cells of the skin site, which cells subsequently react with toxic factors produced by the interaction of the intravenously injected filtrate with the blood serum. Others believe that the lesion results from a vascular allergy, an accelerated Arthus phenomenon (6), or from some peculiar altered reactivity of the blood vessels (7, 8), which must be differentiated from anaphylaxis. Finally, Kielanowski and Selzer (9) concluded, because the changes in the

skin produced by the shocking injections of filtrate are restricted to the blood vessels, that the reaction is due to a "biatropic" effect of the filtrate, whereby excessive dilatation of the blood vessels leads to hemorrhage.

Information about the changes in the permeability of the blood vessels during the development of the Schwartzman reaction should help to determine the various factors controlling its development. Schwartzman (10) has demonstrated that the reaction will occur in the lung, and, inasmuch as both vascular and exudative reactions can be observed simultaneously in separated areas of the lung, I chose this organ in which to study the vascular reactions in the Schwartzman phenomenon.

MATERIALS AND METHODS

Animals. Adult male rabbits weighing from 4 to 5 pounds each were used throughout the course of the experiments. All rabbits were isolated in their cages for from one to two weeks before injection, to determine the absence of pneumonic infections.

Injection materials. A filtrate was prepared from a standard strain of *B. typhosus* according to the method described by Schwartzman (11).

Injection methods. Three cubic centimeters of a filtrate of *B. typhosus* were injected directly into the trachea through a small incision in the neck. For the "shocking dose" an intravenous injection of 4 cc. of the filtrate was made into the marginal ear vein.

Fixation and sectioning. Tissues were fixed in formol-Zenker solution. In some cases the fixation was done intratracheally with the lungs in situ, in order to inflate the alveoli. All tissues were embedded in celloidin and stained with Maximow's hematoxylin-eosin-Azur II.

Criteria for measuring the degree of reaction. In several instances, the sections examined failed to show any reaction to the various types of injection. This might be due to the lack of reactivity of individual animals to the filtrate, but it is more probably due to the failure of the intratracheally injected filtrate

to reach those portions of the lung from which the sections were taken. In such cases the reaction was recorded as negative. In those sections showing positive reactions an arbitrary standard of one to four plus was adopted with which to evaluate the degree of change within the blood vessels and the amount of exudate in the alveolar spaces.

HISTOLOGICAL CHANGES IN THE LUNG FOLLOWING INTRATRACHEAL INJECTIONS OF THE FILTRATE OF *B. TYPHOSUS* AND FOLLOWING INTRATRACHEAL INJECTIONS COMBINED WITH INTRAVENOUS INJECTIONS OF FILTRATE

Shwartzman (12) showed that the reaction to intravenously injected filtrate will not occur until eight to eighteen hours have elapsed between the "preparatory injection" and the "shocking injections," and that the reactivity in the prepared site reaches its peak at twenty-four hours. Gerber (3, 4) demonstrated that the injection of the filtrate into the skin and lymph node produces an immediate inflammatory reaction, and that the active preparatory factor can be neutralized by an immune serum without altering the inflammatory reaction itself. This suggests that some change occurs in the prepared site independent of the ordinary processes of inflammation, and that a period of several hours is required for its development. In an attempt to discover the changes which occur in this period, these experiments were divided into three time intervals. For the first time interval animals were killed four hours after the intratracheal injection of the filtrate of *B. typhosus* so that the immediate reaction of the lungs might be studied at a time when they are not reactive, presumably, to the intravenous injection of filtrate. In the second period, animals were killed twenty-four hours after the intratracheal injection. The changes in the lung were compared with those found at four hours after the intratracheal injection, in order to determine what histologic alterations had occurred in the blood vessels and alveoli, during the period in which the reactivity of the prepared site had developed. In the third period animals were killed fifteen minutes to five hours after the intravenous injection of the "shocking dose" of filtrate into

rabbits which had been given an intratracheal injection of the "preparatory dose" of filtrate twenty-four hours before. The lungs of these animals were studied to determine what changes occur following the reaction of the prepared site with the "shocking dose." By observing differences in the exudate and in the blood vessels produced by the injection of the "shocking dose," the reactive component of the lung might be determined.

The lungs of the animals killed four hours after the intratracheal injection of the filtrate of *B. typhosus* contained, grossly, numerous small areas of hyperemia in the posterior portions of all lobes. The cut surfaces were wet, with many small hyperemic areas. Histologically, there was a diffuse exudation of granulocytes in the alveolar spaces, with marked engorgement of the capillaries. In contrast, the lungs removed twenty-four hours after the intratracheal injection of filtrate exhibited a less marked infiltration of granulocytes into the alveolar spaces and less conspicuous capillary engorgement. The alveoli contained large numbers of septal cells, many of which contained phagocytosed granulocytes, and many of the granulocytes were undergoing karyorrhexis or had pyknotic nuclei. The phagocytes of the alveolar walls were swollen and many were budding off into the alveolar spaces. The bronchi contained granulocytes and erythrocytes. In the animals receiving the "shocking injection" of filtrate the major changes were confined to the blood vessels. There was a widespread collapse of the alveolar spaces around a small amount of exudate. When the alveolar spaces were inflated by intratracheal fixation, the exudate seemed to be identical in all respects to that seen in the lungs twenty-four hours after the intratracheal injection of filtrate alone. The capillaries were dilated and packed with granulocytes, and the arterioles and venules were occluded with numerous polymorphonuclear thrombi. The endothelium was swollen and disrupted. These findings suggest that the pulmonary tissues are most reactive to the intravenous injection of filtrate at a time when the inflammatory reaction is receding. Histologically, there was no evident cause of the hypersensitiveness to the "shocking dose." The marked changes in the lung produced by the intravenous

injection of the "shocking dose" point to an intravascular site for the reaction of the "shocking dose" with the prepared tissues in the lung. There was a marked reaction within the blood vessels, without apparent exudation into the alveolar spaces, which produced an alteration in the lining of the blood vessels with a widespread thrombosis. In the absence of any histologic evidence of altered permeability of the blood vessels, these changes warrant the assumption that the injected filtrate reacts with altered or hypersensitive elements of the blood vessels.

FIXATION OF BLOOD-BORNE BACTERIA IN THE LUNGS FOLLOWING
INTRATRACHEAL INJECTIONS OF THE FILTRATE OF *B. TYPHOSUS*
AND FOLLOWING INTRATRACHEAL INJECTIONS COMBINED WITH
INTRAVENOUS INJECTIONS OF THE FILTRATE

A. *Fixation of Staphylococcus aureus.* It was pointed out in the previous section that the inflammatory reaction which is found in the lungs four hours after the intratracheal injection of the filtrate of *B. typhosus* is receding twenty-four hours after the intratracheal injection, at a time when the prepared lung is most reactive to an intravenous injection of filtrate. When the exudate, which was present twenty-four hours after the intratracheal injection of filtrate, was compared with that which was present after the injection of the "shocking dose," there was no change between the two periods. This led to the conclusion that the reaction between the intravenously injected filtrate and the prepared lung did not increase the permeability of the pulmonary vessels. In addition, the "shocking dose" caused a widespread thrombosis of arterioles and venules, congestion of capillaries with granulocytes, and a disruption and swelling of the endothelium. From these changes, it was concluded that the reaction occurred within the blood vessels and that the underlying cause of the hemorrhagic congestion of the Shwartzman reaction is an alteration of the adhesive properties of the endothelium, with the hemorrhage secondary to the thrombosis.

Since the reaction to the "shocking dose" occurs within the blood vessels without evidence of any change within the alveoli, there should be no alteration in permeability to blood-borne

particles twenty-four hours after the preparatory injection. Furthermore, the altered adhesive properties of the blood vessels should fix blood-borne particles within the blood vessels following the administration of the "shocking dose." To determine these points, bacteria were injected intravenously into four groups of animals. In the first group *Staphylococcus aureus* was injected intravenously into rabbits four hours after an intratracheal injection of the filtrate of *B. typhosus*. The lungs of these animals were studied to determine whether there is any altered adhesive property in the lining of the blood vessels as a result of the simple inflammation present at this time, and to determine whether the increased permeability, seen histologically, applies to foreign particles in the blood stream. The second group of animals received intravenous injections of *Staphylococcus aureus* twenty-four hours after the intratracheal preparatory injection of filtrate in order to determine whether there is an altered permeability to blood-borne materials, and whether there are any changes in the adhesive properties of the endothelium, at the time when the prepared site is reactive to the "shocking dose." The third group received intravenous injections of *Staphylococcus aureus* thirty minutes after the administration of the "shocking dose" in animals which had received the preparatory injection twenty-four hours before the "shocking dose." The fourth group, without previous injections of filtrate, were injected intravenously with *Staphylococcus aureus* to serve as normal controls. All animals were killed 4 to 7 hours after the injection of bacteria.

A standard strain of *Staphylococcus aureus* was used. One cubic centimeter of a twenty-four hour broth culture of the organism was injected intravenously. Broth cultures were used to avoid any clumping that might occur in resuspending the bacteria in salt solution. The method for determining the number and site of the bacteria localized in the lung was to incubate the lungs for twenty-four hours, and to observe the number and site of the colonies found in sections of the lung. The lungs were removed aseptically and incubated twenty-four hours at 37°C. A block was cut from each lobe, fixed in formol-Zenker

solution, and embedded in celloidin. Two sections were cut from each block and stained with hematoxylin-eosin-Azur II. The number of colonies in each slide was counted and the total for all the slides from each lung computed. The total area of the sections from each lung was computed and the total number of colonies in the sections converted to the number of colonies per 100 sq. cm. of slide area.

Four hours after the injection of the filtrate of *B. typhosus*, the bacteria were found within the alveolar spaces. The average number of definite colonies per lung in eleven rabbits was 274 colonies per 100 sq. cm. Twenty-four hours after the intratracheal injection of filtrate, there were occasional colonies found within the alveolar spaces and none in the blood vessels. The average number of colonies per lung in ten rabbits was 8.3 colonies per 100 sq. cm. In the animals receiving the intravenous injection of bacteria thirty minutes after the "shocking dose," the bacterial colonies developed almost entirely within the capillaries and smaller blood vessels, with only an occasional colony within the alveolar spaces. The average number of colonies per lung in thirteen rabbits was 1582 colonies per 100 sq. cm. In the normal rabbits, receiving no previous injections of filtrate, the colonies were within small blood vessels and the average number for twelve rabbits was 74.5 colonies per 100 sq. cm. The largest number of colonies developed in the animals which had received the "shocking dose," and these were confined to blood vessels.

Blood-borne bacteria are localized in the lung four hours after the intratracheal injection of the filtrate of *B. typhosus* because of an increased permeability in the pulmonary vessels which allows the bacteria to enter the alveolar spaces. Twenty-four hours after the intratracheal injection of filtrate, when the inflammatory response to the filtrate is subsiding, there is a slight alteration in the permeability of the pulmonary vessels so that only occasional bacteria enter the alveolar spaces, and there is no tendency to fix bacteria in the blood vessels. At this period, when the reactivity of the prepared site is at its peak (12), materials injected intravenously do not reach the alveolar spaces in appreciable quantities, and any reaction in the prepared site

occurs within the blood vessels. Following the injection of the "shocking dose," there is an alteration of the lining of the blood vessels so that bacteria are fixed within them. This might be due to the congestion of the blood vessels, but, when one considers that there is a similar congestion in the lungs four hours after the intratracheal injection without any fixation of the bacteria within the blood vessels, this does not appear to be an adequate explanation. There appears to be an additional change in the lining of the blood vessels which causes bacteria to adhere to the walls. The nature of this change is not clear. The reaction "per se" does not alter the permeability of the capillaries.

B. Fixation of B. typhosus in the lungs of animals following the administration of the "shocking dose" of the filtrate of B. typhosus. Several workers (6) have suggested that the reaction is the result of an allergic alteration of the prepared site. If this were the case, the reaction of the "shocking dose" with the prepared site would represent a desensitization of the cells in the area. Hopkins and Parker (16) have demonstrated that a state of reactivity to bacteria can be developed within twenty-four hours. If the reaction is due to the formation of antibodies at the prepared site with a subsequent antigen-antibody reaction, there should be an increased tendency to fix specific organisms over that of non-specific organisms (17, 18). To determine whether this relationship holds for the Schwartzman reaction, suspensions of *B. typhosus* were injected intravenously thirty minutes after the administration of the "shocking dose" and the number of organisms found in the lungs compared with those found after the injection of *Staphylococcus aureus*. The technic for determining the number of bacteria localized was the same as that described in Section A.

The number of colonies of *B. typhosus* found per lung in seventeen rabbits was 1321 colonies per 100 sq. cm. The colonies were situated within blood vessels. The number of colonies of *Staphylococcus aureus* found under similar conditions in Section A was 1582 colonies per 100 sq. cm. There is no significant difference between the number of specific organisms and non-specific organisms fixed in the lungs after the reaction of the "shocking

dose" with the prepared lung. If there were specific antibodies present in the prepared site, the specific organisms should be more readily fixed than the non-specific organisms (17, 18). There is no evidence in these experiments to indicate that such is the case.

FIXATION OF INDIA INK IN THE LUNGS FOLLOWING INTRATRACHEAL INJECTIONS OF THE FILTRATE OF *B. TYPHOSUS* AND INTRATRACHEAL INJECTIONS COMBINED WITH INTRAVENOUS INJECTIONS OF FILTRATE

In using bacteria to determine an alteration in the adhesive properties of the blood vessels, several difficulties arose. First, the incubation of the lung produced marked autolysis, so that it was impossible to determine the exact site of the bacteria within the wall of the alveolus, and the bacteria could not be seen to be actually adhering to the lining of the blood vessels. Furthermore, there was a possibility of error in counting the colonies from small blocks. To overcome these difficulties, it was decided to use India ink as an indicator.

The experiment was divided into four groups. Each animal received 8 cc. of a 5 per cent suspension of a standard India ink. In the first group, the India ink was injected intravenously four hours after the intratracheal injection of the preparatory dose of the filtrate of *B. typhosus*, to demonstrate the increase in capillary permeability. In the second group, the India ink injections were made twenty-four hours after the injection of the preparatory dose. In the third group, the India ink was injected thirty minutes after the administration of the "shocking dose" into animals which had received the preparatory injection twenty-four hours before the "shocking dose." In the fourth group, the India ink was injected into normal animals, receiving no previous injections, to determine the amount of and the site of the ink localized in the normal lung. All animals were killed twenty-four hours after the injection of the India ink. The gross fixation of the ink was recorded and the lungs were fixed in Romeis solution (saturated mercuric chloride, 5 per cent trichloroacetic acid, and concentrated neutral formalin, in the proportions of 25:20:5), embedded in celloidin, and stained with eosin and

hematoxylin-eosin. In measuring the amount of ink in the lungs, the light grey distribution seen, grossly, in the normal lungs was designated as one plus. Diffuse deep shades of grey-black were called two plus localization, small distinct black areas were called three plus, and large sharply defined black areas were judged to represent the maximum, or four plus, fixation.

In the group which was injected intravenously with India ink four hours after the injection of the preparatory injection, the ink was confined, grossly, to sharply outlined black areas in the posterior portions of all lobes. Seven of the twelve rabbits which were injected revealed a four plus fixation of the ink, four exhibited three plus, and one exhibited one plus. Histologically, most of the ink was found in macrophages and granulocytes in the alveolar exudate. A small amount remained inside blood vessels, but was not adherent to the walls, and in macrophages of the alveolar walls. In the group which received the ink injections twenty-four hours after the preparatory dose of filtrate, the ink, grossly, was distributed uniformly over the entire lung, producing a gray-black color. In the twelve rabbits which were injected seven exhibited one plus fixation, two exhibited two plus, and two exhibited three plus. One died immediately after the ink injection. Histologically, the ink was found in macrophages in the alveolar walls, with occasional particles in the cells of the alveolar exudate. The particles remaining in the blood vessels were either in granulocytes or free in the lumen, and did not adhere to the walls of the vessels. In the group receiving the intravenous injections of ink thirty minutes after the injection of the "shocking dose," the ink, grossly, was found in large, sharply defined, black areas in the posterior portions of all lobes. Of the twelve animals which were injected, seven exhibited four plus fixation, three exhibited three plus, and two died following the injection of the ink. Histologically, most of the ink was fixed within the blood vessels, lying against the endothelium as though it were plastered there. Occasional particles were found in the cells of the alveolar exudate and in the macrophages of the alveolar walls. In the controls, which had not received previous injections of filtrate, the ink, grossly, was distributed uniformly

over all lobes, and, histologically, was found in the alveolar macrophages. These results clearly substantiate the findings of the previous experiments and clarify many of the points. Although there was an inflammatory alteration of permeability in the pulmonary capillaries four hours after the intratracheal injection of the filtrate of *B. typhosus*, there was no alteration of the adhesive properties of the endothelium. The increased permeability had disappeared twenty-four hours after the preparatory injection, which is the period when the prepared site is most reactive to the injection of the "shocking dose" of filtrate (12). There was no tendency to fix the ink along the walls of the vessels at this time. Apparently the increased adhesive qualities of the endothelium are produced in the reaction of the "shocking dose" with the prepared site. Inasmuch as the prepared site will not react with the "shocking dose" four hours after the preparatory injection, when there is a marked increase in permeability of the pulmonary vessels, it appears that the reaction is not due to the primary toxicity of the filtrate. Since the reaction does occur when there is no appreciable increase in permeability of the pulmonary vessels, it must occur within the blood vessels. The fact that the major changes produced by the reaction are confined to the blood vessels confirms this view. The ink, which was fixed after the reaction of the "shocking dose," adhered to the endothelial cells. This suggests that the sensitized cells in the reaction may be the endothelial cells, or the reticulo-endothelial cells which are intimately associated with the blood vessels.

THE PRODUCTION OF EMBOLIC PNEUMONIAS BY THE INTRAVENOUS
INJECTION OF BACTERIA IN ANIMALS WHICH HAVE RECEIVED
INTRATRACHEAL INJECTIONS OF THE FILTRATE OF *B. TYPHOSUS*
COMBINED WITH INTRAVENOUS INJECTIONS OF FILTRATE

It has been shown that intravenously injected bacteria are fixed within the pulmonary blood vessels of animals which have received preparatory and shocking injections of a filtrate of *B. typhosus*. The fixation of *Staphylococcus aureus* was as great as the fixation of *B. typhosus*. The bacteria are apparently fixed in

the blood vessels by an increased adhesive quality of the endothelium of the vessels, which is produced by the reaction of the "shocking dose" with the prepared site in the lung. To determine whether these bacteria will subsequently produce further inflammatory changes in the lungs, the following experiments were done. Four groups of animals were studied. In the first group, the animals received intratracheal preparatory injections of the filtrate of *B. typhosus* which were followed in twenty-four hours by intravenous injections of the "shocking dose" of filtrate. These animals were killed three days after the injection of the "shocking dose" to determine what changes are present at that time as the result of the injections of filtrate. The second group received intravenous injections of suspensions of *B. typhosus*, which were given thirty minutes after the injection of the "shocking dose" in animals which had previously received the "preparatory" injection. The third group received intravenous injections of a suspension of *Staphylococcus aureus* thirty minutes after the injection of the "shocking dose" of filtrate in previously "prepared" animals. The fourth group, without previous injections of filtrate, received intravenous injections of *Staphylococcus aureus* or *B. typhosus*, to serve as controls. The last three groups were killed three days after the injection of bacteria.

Three cubic centimeter of a filtrate of *B. typhosus* were used for the intratracheal injections, and 4 cc. of the filtrate for the intravenous injections. One cubic centimeter of twenty-four-hour broth cultures of *B. typhosus* and *Staphylococcus aureus* were used for the intravenous injections of bacteria. The lungs were fixed in formol-Zenker solution, embedded in celloidin, and stained with hematoxylin-eosin-Azur II.

The lungs of those rabbits which received only the preparatory and shocking injections of filtrate, grossly, appeared normal. Histologically, the alveolar walls were normal, the capillaries contained a few granulocytes, many of the arterioles and venules were occluded by polymorphonuclear thrombi, and there were many septal cells in the alveolar spaces. The perivascular lymph channels contained granulocytes and septal cells. The lungs of the animals which received intravenous injections of

B. typhosus after the injection of the preparatory and shocking doses of filtrate, grossly, contained areas of consolidation, which varied from complete consolidation of one lobe to multiple consolidations, varying in diameter from 5 mm. to 1 cm. Histologically, there were typical areas of lobular pneumonia with an alveolar exudate of granulocytes, fibrin, and edema fluid. The consolidated areas were found either subpleurally or in the region of the hilum. Of the ten rabbits injected, eight exhibited consolidations and two were normal. The lungs of the animals which were injected with *Staphylococcus aureus* after the injection of the preparatory and shocking doses of filtrate, grossly contained multiple small abscesses. The lungs of the animals which received only an intravenous injection of bacteria were normal.

SUMMARY AND CONCLUSIONS

The Shwartzman reaction to a filtrate of *B. typhosus* was studied in the lungs of rabbits. The following findings were revealed in the experiments:

1. The intratracheal injection of a filtrate of *B. typhosus* produces an acute alveolitis. Four hours after the intratracheal injection intravenously injected bacteria and India ink are localized in the alveolar spaces because of an inflammatory alteration of permeability of the pulmonary blood vessels.

2. Twenty-four hours after the intratracheal injection of filtrate the inflammatory reaction is subsiding. At this period, when the reactivity of the prepared site in the Shwartzman reaction is at its peak, there is no alteration of permeability when measured by intravenous injections of bacteria or India ink.

3. When the "shocking" dose of filtrate is given intravenously into animals which have been previously prepared by an intratracheal injection of filtrate, the changes produced by the "shocking dose" are confined to the pulmonary blood vessels, and consist of widespread thrombosis of arterioles and venules, dilatation of the capillaries, engorgement of the capillaries with granulocytes, and disruption and swelling of the endothelium. There is no alteration of the alveolar exudate from that seen twenty-four hours after the preparatory injection. When bacteria or India

ink are injected intravenously at this period, they are fixed within the blood vessels, and the India ink is plastered to the endothelium. The reaction is non-specific, for there is equal fixation of *Staphylococcus aureus* and *B. typhosus* in the lungs at this time.

4. When bacteria were injected intravenously into rabbits which had received both the preparatory injection and the shocking injection of a filtrate of *B. typhosus*, embolic pneumonias were present three days after the injection of bacteria. *B. typhosus* produced a lobular consolidation, and *Staphylococcus aureus* produced abscesses.

From these findings it is concluded that the Schwartzman reaction occurs within the blood vessels of the lung as the result of an alteration of the blood vessels by the preparatory injection and that the hemorrhagic congestion that characterizes the Schwartzman reaction is secondary to the widespread thrombosis. The non-specific fixation of the bacteria indicates that the reaction is not due to an antigen-antibody reaction.

I wish to express my appreciation of the aid and advice Dr. Paul R. Cannon has given me in the course of these experiments.

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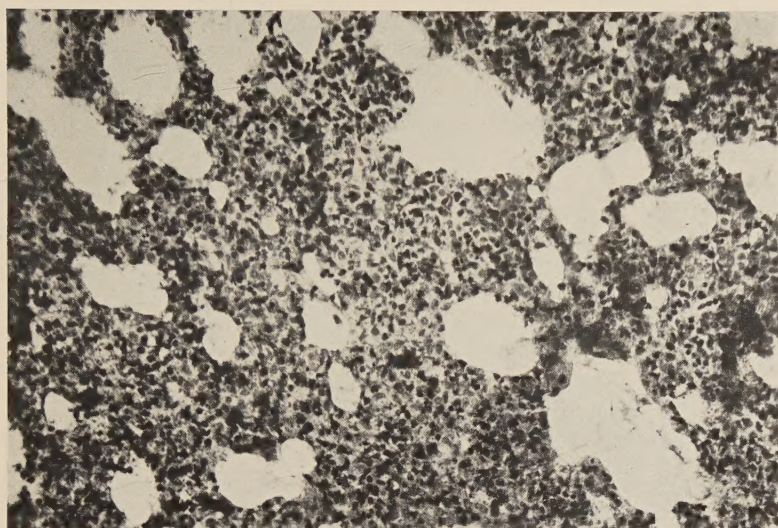


FIG. 1. REACTION OF THE LUNG FOLLOWING PREPARATORY AND SHOCKING INJECTIONS OF A FILTRATE OF *B. TYPHOSUS*

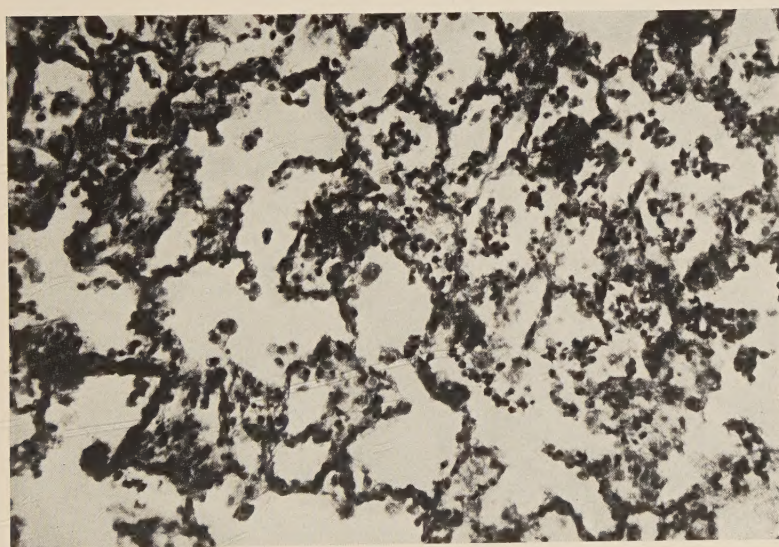


FIG. 2. REACTION IN THE LUNG TWENTY-FOUR HOURS AFTER THE INTRATRACHEAL INJECTION OF 3 CC. OF A FILTRATE OF *B. TYPHOSUS*

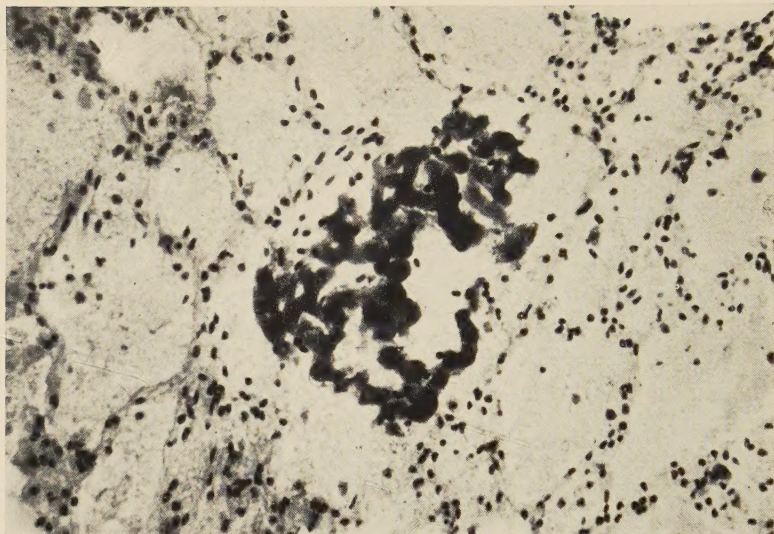


FIG. 3. LOCALIZATION OF *B. TYPHOSUS* IN THE CAPILLARIES OF THE LUNG FOLLOWING THE INTRAVENOUS INJECTION OF 1 CC. OF A TWENTY-FOUR HOUR BROTH CULTURE OF *B. TYPHOSUS* INTO A RABBIT WHICH HAD PREVIOUSLY RECEIVED PREPARATORY AND SHOCKING INJECTIONS OF A FILTRATE OF *B. TYPHOSUS*

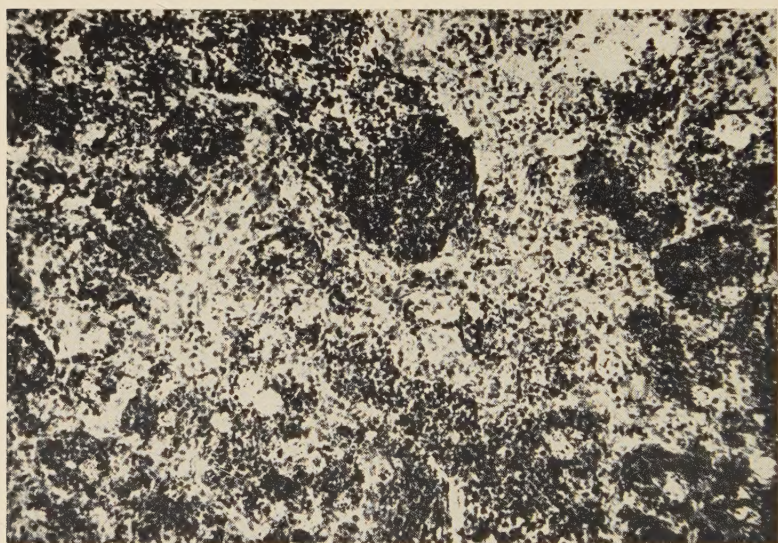


FIG. 4. EMBOLIC PNEUMONIA IN A LUNG REMOVED THREE DAYS AFTER THE INTRAVENOUS INJECTION OF 1 CC. OF A TWENTY-FOUR-HOUR BROTH CULTURE OF *B. TYPHOSUS* INTO A RABBIT THIRTY MINUTES AFTER THE INJECTION OF THE SHOCKING DOSE OF A FILTRATE OF *B. TYPHOSUS* IN A PREVIOUSLY PREPARED ANIMAL

